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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,238	03/29/2004	Kishore K. Wary	D6563	3362

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/812,238	WARY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,14,15,20,21 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,14,15,20,21 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 1/13/06, is acknowledged.

2. Claims 8-9, 14-15, 20-21 and 32 are pending and under examination as they read on a method of inhibiting cell-cell interaction, a method of treating a patient having a pathological condition and a method of inhibiting angiogenesis and the formation of capillaries in patient with antibody directed against a peptide comprises CRGDD sequence, angiogenesis, inflammation and tumor growth as the species.

3. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. The specification on page 34, table 1 has described sequences that each must have a sequence identifier. Correction is required.

Applicant indicates that the previous amendment to the specification filed on 8/22/05 include SEQ ID NOs for the sequences of the peptides listed in the table. However, the Examiner was not able to find the replacement for page 34 as indicated on said amendment.

4. Claim 32 is objected to for the following informalities: the article "an" should be inserted before the word "antibody".

5. In view of the amendment filed on 1/13/06, only the following rejections are remained.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 8-9, 14-15, 20-21 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting cell-cell interaction or a method of treating inflammation or angiogenesis comprising contacting the cells with an antibody directed against the sequence consisting of SEQ ID NO: 41 or the SEQ of SEQ ID NO: 2, wherein said peptide is derived from human VCIP of SEQ ID NO: 14, wherein said antibody blocks binding of $\alpha v\beta 3$ and $\alpha 5\beta 1$ integrins to VCIP, thereby inhibiting the cell-cell interaction. does not reasonably provide **enablement** for a method of inhibiting cell-cell interaction comprising contraction the cells with an antibody directed against a peptide "with" any sequence fo SEQ ID NO: 41 or with any sequence of SEQ IN NO: 2, that is derived from any "cell surface VCIP", wherein said contact with the antibody blocks binding of "integrins" the cell surface VICP, thereby inhibiting the cell-cell interaction, in claim 8, wherein said cell-cell interaction is mediated by any "integrin ligand" in claim 9, wherein said cell-cell interaction contributes to inflammation, angiogenesis or a combination thereof in claim 14, or a method of treating a patient with any pathological condition caused by integrin-mediated cell-cell interaction, comprising administering to said patient an antibody directed against a peptide with any

sequence of SEQ ID NO:41 or SEQ ID NO: 2 that is derived from any "cell surface VCIP", wherein said antibody blocks binding of integrin to the cell surface VCIP, thereby treating the patient with the pathological condition caused by the integrin-mediated cell-cell interaction in claim 15, wherein said cell-cell interaction contributes to inflammation, angiogenesis or a combination thereof in claim 20, wherein said pathological condition is "tumor growth", inflammation, angiogenesis or a combination thereof in claim 21 or a method of inhibit angiogenesis and the formation of capillaries in a patient in need of such a treatment comprising administering to said patient a pharmacologically effective amount of an antibody against a peptide with any sequence of SEQ ID NO: 41 or SEQ ID NO: 2 that derived from any "VCIP", wherein said antibody inhibits any "integrin-mediated cell-cell interaction" thereby inhibiting angiogenesis and the formation capillaries in the patient in need of such a treatment in claim 32. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

Applicant's arguments, filed 1/13/06, have been fully considered, but have not been found convincing.

Regarding the open language use (i.e., has and comprise), Applicant submits that independent claims 8, 15 and 32 now recite the antibody used in the method is directed against peptides having specific sequences such as SEQ ID NO: 41 or 2 that are derived from VCIP.

However, there is no structural component feature for VCIP for the skilled in the art to determine the peptide to which the claimed antibody binds. The skilled in the art would not know what species of VCIP to use (e.g., human, mouse, rat, among other). Further, the specification identifies only $\alpha v\beta 3$ and $\alpha 5\beta 1$ integrins to bind VCIP, the skilled in the art would not know what other integrins interacts with VCIP can be inhibited with the claimed antibodies. Furthermore, the specification is not enabled for treating any pathological condition or inhibiting any cell-cell interaction.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 8-9 and 14 stand rejected under 35 U.S.C. 102(b) as being anticipated by Vassilev et al (Blood. 1999 Jun 1;93(11):3624-31), as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Action mailed 9/30/05.

Applicant's arguments, filed 1/13/06, have been fully considered, but have not been found convincing.

Applicant argues that Vassilev et al teach that the antibody was directed against a 10-amino acid peptide containing the RGD motif (page 3624, 2nd col, last para). Applicant concludes that Vassilev et al neither teach that the antibody was directed against the 5-amino peptide (SEQ ID NOL 41) or 20 amino acid peptide (SEQ IN NO: 2) nor does it teach that the peptide was derived from VCIP as disclosed by the instant invention. Applicant further concludes that Vassilev et al does not teach each and every element of the claim because the reference does not each the same product used in the claimed method. Applicant states that whether an antibody generated using the above-mentioned peptides would block the binding of integrins to cell surface VCIP is not inherent. Applicant further contends that independent claim 8, and its dependent claims 9 and 14 are not anticipated by Vassilev et al.

However, Applicant's argument attempts to limit the referenced antibody to a "10-amino acid peptide containing the RGD motif" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That is an antibody "cross-reacts", i.e., binds to more than one protein sequence, does not mean that the antibody does not "bind" with both proteins.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 15, 20-21 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,807,819 in view of U.S. Pat. No. 5,567,440 and Vassilev et al as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Action mailed 9/30/05.

Applicant's arguments, filed 1/13/06, have been fully considered, but have not been found convincing.

Applicant argues that Vassilev's anti-RGD antibody generated against a 10-amino acid peptide and not the specific VCIP-derived peptide as taught by the instant invention. Applicant argues that the prior art references combined do not teach or suggest all the limitation of the instant

claim nor do they motivate one of ordinary skill in the art to arrive at the instant invention with reasonable expectation of success.

However, Applicant's argument attempts to limit the referenced antibody to a "10-amino acid peptide containing the RGD motif" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That is an antibody "cross-reacts", i.e., binds to more than one protein sequence, does not mean that the antibody does not "bind" with both proteins. Regarding motivation to combined the references, it is noted that while there is no requirement that a motivation to make the modification be expressly articulated, the `440 patent provide a clear motivation as to why the skilled artisan would substitute the CRGDDVC cyclic peptide taught by the `819 patent with anti-RGD antibody taught by Vassilev *et al* in a method of inhibiting angiogenesis in a subject. That is because routes to the interruption of cell-cell interactions typically involve competitive inhibition of these receptor-ligand interactions with either receptor antagonists (e.g., cyclic RGD peptides), antibodies or other competitors. Further, a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding element disclosed in the specification. *Caterpillar Inc. v. Deere & Co.*, 224 F.3d 1374, 56 USPQ2d 1305 (Fed. Cir. 2000); *Al-Site Corp. v. VSI Int' l, Inc.*, 174 F.3d 1308, 1316, 50 USPQ2d 1161, 1165 (Fed. Cir. 1999); *Chiuminatta Concrete Concepts, Inc. v. Cardinal Indus. Inc.*, 145 F.3d 1303, 1309, 46 USPQ2d 1752, 1757 (Fed. Cir. 1998); *Lockheed Aircraft Corp. v. United States,* 193 USPQ 449, 461 (Ct. Cl. 1977); *Data Line Corp. v. Micro Technologies, Inc.*, 813 F.2d 1196, 1 USPQ2d 2052 (Fed. Cir. 1987).

12. The following new ground of rejection is necessitated by the amendment filed on 1/13/06.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 8-9, 14-15, 20-21 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The recitation "a peptide with a sequence of SEQ ID No:41, or with a sequence of SEQ ID NO:2" recited in claims 8, 15 and 32 is ambiguous. It is unclear whether the peptide is attached (added) to, derive from, comprising or consisting of SEQ ID NO: 2 or 41.

15. Claims 14, 20, and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "inflammation, angiogenesis or a combination thereof" claimed in claim 14 and 20 and the phrase "tumor growth, inflammation, angiogenesis or a combination thereof" in claim 21 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 1/13/06 does not point to the specification for support for the newly added limitations "inflammation, angiogenesis or a combination thereof" as claimed in claims 14 and 20, and "tumor growth, inflammation, angiogenesis or a combination thereof" in claim 21. However, the specification does not provide a clear support for such combination. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 23, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner